Title

The global distribution of Bacillus anthracis and associated anthrax risk to humans, livestock and wildlife.

Journal

Nature microbiology, 4(8)

ISSN

2058-5276

Authors

Carlson, Colin J
Kracalik, Ian T
Ross, Noam
et al.

Publication Date

2019-08-01

DOI

10.1038/s41564-019-0435-4

Peer reviewed

nature microbiology

ARTICLES

https://doi.org/10.1038/s41564-019-0435-4

The global distribution of *Bacillus anthracis* and associated anthrax risk to humans, livestock and wildlife

Colin J. Carlson[1,2,15], Ian T. Kracalik[3,4,15], Noam Ross[5], Kathleen A. Alexander[6], Martin E. Hugh-Jones[7], Mark Fegan[8], Brett T. Elkin[9], Tasha Epp[10], Todd K. Shury[11], Wenyi Zhang[12], Mehriban Bagirova[13], Wayne M. Getz[14] and Jason K. Blackburn[3,4*]

***Bacillus anthracis* is a spore-forming, Gram-positive bacterium responsible for anthrax, an acute infection that most significantly affects grazing livestock and wild ungulates, but also poses a threat to human health. The geographic extent of *B. anthracis* is poorly understood, despite multi-decade research on anthrax epizootic and epidemic dynamics; many countries have limited or inadequate surveillance systems, even within known endemic regions. Here, we compile a global occurrence dataset of human, livestock and wildlife anthrax outbreaks. With these records, we use boosted regression trees to produce a map of the global distribution of *B. anthracis* as a proxy for anthrax risk. We estimate that 1.83 billion people (95% credible interval (CI): 0.59–4.16 billion) live within regions of anthrax risk, but most of that population faces little occupational exposure. More informatively, a global total of 63.8 million poor livestock keepers (95% CI: 17.5–168.6 million) and 1.1 billion livestock (95% CI: 0.4–2.3 billion) live within vulnerable regions. Human and livestock vulnerability are both concentrated in rural rainfed systems throughout arid and temperate land across Eurasia, Africa and North America. We conclude by mapping where anthrax risk could disrupt sensitive conservation efforts for wild ungulates that coincide with anthrax-prone landscapes.**

Anthrax is a zoonotic disease caused by the Gram-positive bacterium *Bacillus anthracis*, a generalist soil-transmitted pathogen found on every inhabited continent[1], and several islands including Haiti and parts of the Philippines and Indonesia. Worldwide, an estimated 20,000 to 100,000 cases of anthrax occur annually, mostly in poor rural areas[2]. In clinical presentations of anthrax, case fatality rates are a function of exposure pathway. Respiratory exposure from spore inhalation is important in the context of bioterrorism, but is highly uncommon, and accounts for a negligible fraction of the global burden of anthrax cases. Cutaneous exposure to *B. anthracis* accounts for the majority of human cases worldwide, and typically presents with low mortality; gastrointestinal exposure accounts for the remainder and presents with intermediate to high fatality rates. Cutaneous and gastrointestinal cases of anthrax are most commonly caused by handling and slaughtering infected livestock, or butchering and eating contaminated meat; untreated gastrointestinal cases probably account for most human mortality from anthrax[1–3].

Human mortality from anthrax is driven by ecological dynamics at the wildlife–livestock interface[4]. In nature, the enzootic cycle of anthrax is characterized by a combination of long-term spore persistence in soil, and an obligate-lethal transmission route, primary in herbivorous mammals[1,5,6]. Both wild herbivores and livestock are gastrointestinally exposed to *B. anthracis* spores from soil while grazing, become infected, and usually return spores to the soil when they die and decompose[7]. As domesticated and wild herbivores frequently share grazing grounds, wildlife epizootics can lead to downstream infections in livestock and humans. In some regions, anthrax is hyperendemic, and cases follow regular seasonal trends; in other regions, the disease re-emerges in major epidemics after years or decades without a single case[6]. Environmental persistence facilitates these unusual dynamics; under optimal conditions, *B. anthracis* spores are able to persist in the soil for long periods (that is, decades). Alkaline, calcium-rich soils are believed to facilitate sporulation, and therefore drive landscape-level patterns of persistence; these patterns are usually hypothesized to drive the distribution of *B. anthracis* up to the continental scale[1,5].

Global variation in anthrax endemism and outbreak intensity has previously been characterized at extremely coarse scales[8,9], but anthrax is a neglected disease, and its global distribution is still poorly characterized. In total, roughly a dozen studies have used ecological niche models to develop regional (usually national-level) maps of suitability for *B. anthracis* (see Supplementary Table 1). These regional mapping efforts are a critical part of the public health planning process[10], but are primarily conducted in isolation, and the results of these studies have yet to be consolidated and synthesized.

[1]National Socio-Environmental Synthesis Center, University of Maryland, Annapolis, MD, USA. [2]Department of Biology, Georgetown University, Washington, Washington DC, USA. [3]Spatial Epidemiology & Ecology Research Lab, Department of Geography, University of Florida, Gainesville, FL, USA. [4]Emerging Pathogens Institute, University of Florida, Gainesville, FL, USA. [5]EcoHealth Alliance, New York, NY, USA. [6]Department of Fish and Wildlife Conservation, Virginia Tech, Blacksburg, VA, USA. [7]School of the Coast and Environment, Louisiana State University, Baton Rouge, LA, USA. [8]AgriBio, Centre for Agribiosciences, Biosciences Research, Department of Economic Development, Jobs, Transport and Resources, Bundoora, Victoria, Australia. [9]Department of Environment and Natural Resources, Government of the Northwest Territories, Yellowknife, Northwest Territories, Canada. [10]Department of Large Animal Clinical Sciences, Western College of Veterinary Medicine, University of Saskatchewan, Saskatoon, Saskatchewan, Canada. [11]Parks Canada Agency, Saskatoon, Saskatchewan, Canada. [12]Center for Disease Surveillance & Research, Institute of Disease Control and Prevention of PLA, Beijing, China. [13]Scientific Research Veterinary Institute, Baku, Azerbaijan. [14]Department of Environmental Science, Policy, and Management, University of California, Berkeley, Berkeley, CA, USA. [15]These authors contributed equally: Colin J. Carlson, Ian T. Kracalik. *e-mail: jkblackburn@ufl.edu

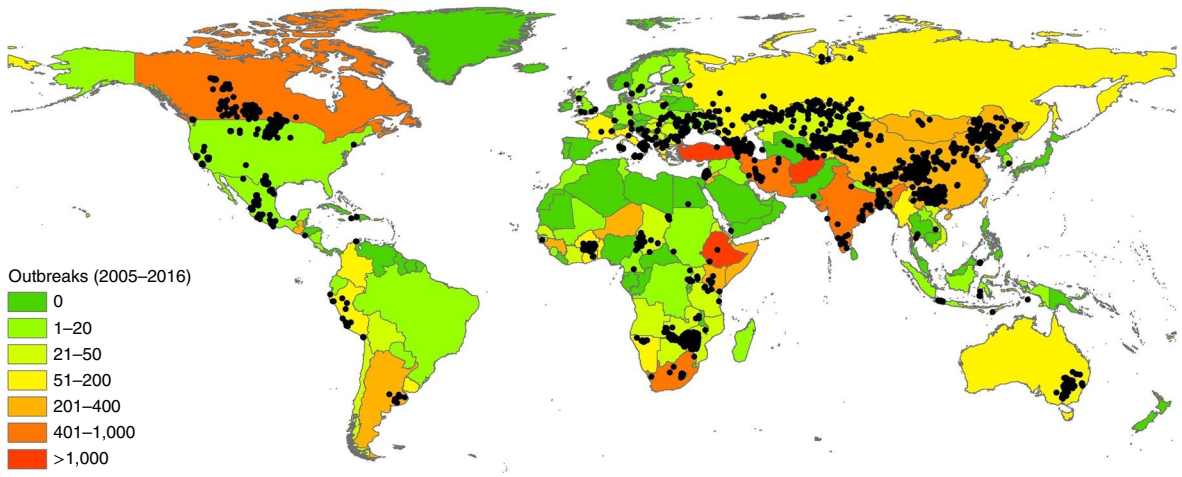

Fig. 1 | Global distrubtion of outbreaks by country and geographic locations of anthrax events. Global database of anthrax occurrences (points) versus outbreaks of anthrax by country (January 2005–August 2016; data digitized from ref. [9]). Black dots represent individual outbreak locations used in predictions.

Furthermore, cross-validation of regional models has only recently been attempted[11], and indicates either limitations in model transferability, or possible genetic or ecological differences underlying distributional patterns of different regions; either way, this highlights the limitations preventing regional models from being scaled up to a global estimate. Moreover, the distribution of anthrax has yet to be modelled in several broad regions where it is nevertheless pervasive, especially Western Europe, the Middle East and South America. Cryptic persistence of *B. anthracis* spores in the soil makes mapping efforts especially challenging, as suitable and endemic regions could go years or potentially decades without a recorded outbreak.

This study consolidates clinical and ecological research on enzootic and epidemic anthrax reports, compiling the largest global database of anthrax occurrences on record to map the global suitability for *B. anthracis* persistence. A total of 5,108 records were compiled describing the global distribution of anthrax across 70 countries (Fig. 1). Here we used a subset of 2,310 of these data points to describe the global distribution and eco-epidemiology of *B. anthracis*, exploring the relationship of anthrax outbreaks to environmental factors including soil characteristics and climate, via boosted regression trees (BRTs) as a tool for species distribution modelling. These maps provide a proxy for anthrax risk. We apply this global anthrax model to provide a first estimate of the global human and livestock populations at risk from anthrax. We compare the distribution of anthrax to that of critically threatened wildlife populations and identify areas where additional or new surveillance is needed to anticipate and prevent rare, but probably catastrophic, threats to wildlife conservation efforts.

Results

Our global ensemble distribution model (Fig. 2) performed very well on validation data (mean area under the curve (AUC) = 0.9244), and regionally matches the well-established distribution of anthrax in China[12], Kazakhstan[13], North America[14] and Australia[15], suggesting that it appropriately captures the global range of *B. anthracis*. These four regions, along with a band of suitability in sub-Saharan Africa around roughly 15° S, represent the most geographically expansive zones of anthrax endemicity, and hotspots of human vulnerability. However, our study also shows that perhaps the majority of the European continent, and a substantial part of the Anatolian peninsula and surrounding region, are also highly suitable for *B. anthracis*. In some cases, high-risk areas match hyperendemic areas, such as Turkey and South Africa; but in other cases (for example, in Ethiopia), predicted areas of suitability were more limited than expected in countries with a high anthrax burden. This may reflect sampling limitations in these areas. For example, Ethiopia is significantly under-represented, despite the high incidence of anthrax outbreaks characterized by high morbidity and mortality[16]; this is at least partially attributable to the country's limited surveillance capacity, overwhelmed by poverty and the high incidence (and co-morbidity) of other neglected tropical and zoonotic diseases[17,18]. However, discrepancies between suitability and incidence also probably reflect regional variation in anthrax control. Where food safety practices prevent exposure and livestock vaccinations are affordable, high anthrax suitability may not translate into high case burdens (supported by the vaccination data in the Supplementary Information); conversely, anthrax morbidity and mortality are usually exacerbated by limited local knowledge about anthrax, limited access to healthcare and conflicting pressures such as food insecurity that force local populations to handle and eat contaminated meat.

Globally, we find that an estimated 1.8 billion people live within anthrax-suitable areas, the vast majority of whom live in rural areas in Africa, Europe and Asia (Table 1). However, most of that population probably has no occupational exposure to infected animals, and direct exposure from the soil has rarely been reported for human cases; in those few reported cases patients had compromised immune systems and unknown or unusual exposure[19]. For a more informative perspective on risk, we estimate that a total of 63.8 million rural poor livestock keepers live in anthrax-affected areas (95% credible interval (CI): 17.5–168.6 million; Table 1), again primarily in Africa and Eurasia. Globally, we found that areas of anthrax risk contain 1.1 billion livestock (95% CI: 404 million–2.3 billion; Table 2), including 320 million sheep (95% CI: 138–622 million), 294.9 million pigs (95% CI: 103–583 million), 268.1 million cattle (95% CI: 87.4–639 million), 211.2 million goats (95% CI: 74.8–453 million) and 0.6 million buffalo (95% CI: 0.16–1.6 million). Although arid and semi-arid ecosystems were a significant source of vulnerable livestock across production systems (especially for cattle), the single most significant across all four groups was rainfed mixed crop/livestock systems in temperate-highland ecosystems, due to the disproportionate contribution from East Asia, especially China (Table 1).

Most livestock at risk of anthrax are unvaccinated in any given year (Fig. 3). As per reported data, an average of 212.8 million live attenuated vaccines for anthrax are manufactured every year (2005–2016) outside the United States (which reports no data but is also a

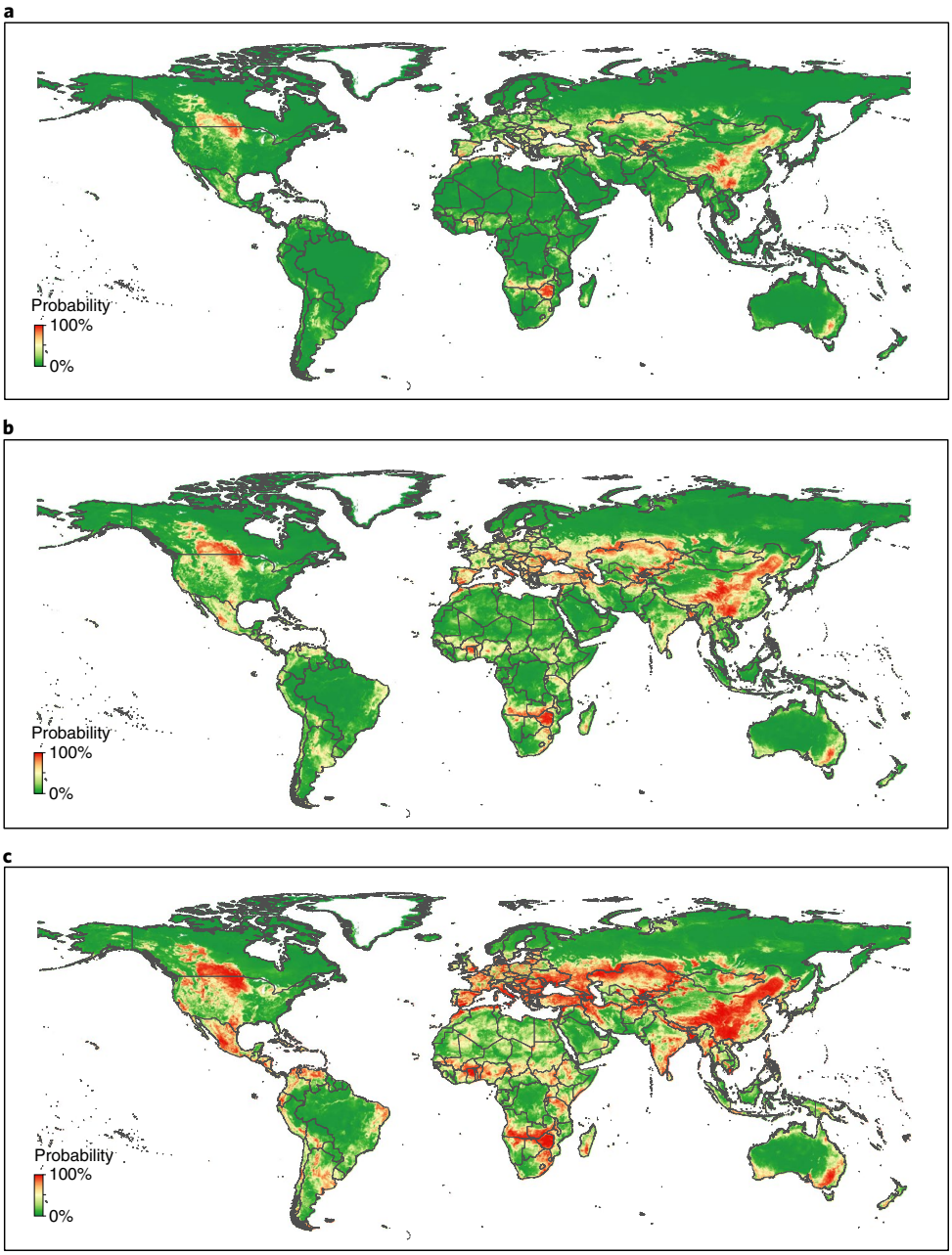

Fig. 2 | Global distribution of *B. anthracis* suitability (probability of occurrence). a–c, The estimate was modelled by an ensemble of 500 BRTs; lower 95% confidence bound (**a**), mean of all 500 models (**b**) and upper 95% confidence bound (**c**).

major manufacturer); on average, 198.2 million doses are used for livestock every year. Compared to the 1.1 billion livestock at risk, vaccine coverage is patchy and regionally variable; roughly 90% of cattle, sheep and goats are annually vaccinated in Eastern Europe and Central Asia, due to a strong legacy of mass vaccination campaigns in the former Soviet Union. On the other hand, vaccination rates are alarmingly low in sub-Saharan Africa (0–6%), East Asia (0–5%) and South Asia (<1%), where more than half of the livestock at risk and 48.5 million rural poor livestock keepers are located. In these regions, livestock vaccination is commonly used reactively after a major outbreak, rather than as a preventative measure[14,20]; improving proactive vaccination in under-vaccinated, hyperendemic countries (in particular Afghanistan, Bangladesh, Ethiopia, South Africa, Turkey and Zimbabwe) could help bring anthrax outbreaks under control[10]. Vaccination may also be less effective than usual for the 31 million livestock and 4.6 million poor livestock keepers in West Africa, where an endemic lineage of *B. anthracis* shares an anthrose-deficiency mutation that has been hypothesized to lead to a vaccine escape[21]. Education campaigns may be more cost-effective than mass vaccination, which is both cost-prohibitive and logistically challenging in inaccessible rural areas. However, livestock keepers may continue to sell contaminated meat to recoup financial losses (which also contributes to under-reporting); this has increased cases in urban settings[22]. In cases of extreme food insecurity, poor populations may eat anthrax-infected meat despite understanding the risks.

Although risk is most commonly measured at the human–agriculture interface, anthrax also has a major ecological impact; while *B. anthracis* is a stable part of some savannah ecosystems, epizootics in other regions can have catastrophic impacts on wildlife

Table 1 | Population at risk (in millions) by region, land use and occupational exposure

Region	Poor livestock keepers	Rural	Peri-urban	Urban	Total
East Asia and the Pacific	5.7	458.5	15.0	162.4	635.9
South Asia	26.6	345.0	1.9	55.1	401.9
Western and Central Europe	0.26	125.3	14.0	79.6	218.8
North Africa and the Middle East	6.6	152.9	6.1	51.7	210.7
Eastern Europe and Central Asia	5.6	112.7	3.4	26.5	142.7
Sub-Saharan Africa	16.2	84.2	1.5	16.6	102.3
Latin America and the Caribbean	2.9	38.1	2.6	42.0	82.7
North America	<0.1	5.6	3.6	21.5	30.8
Australia and Oceania	<0.1	0.74	0.24	0.7	1.76
World total	**63.8**	**1,323.1**	**48.4**	**456.1**	**1,827.5**

Table 2 | Estimated global livestock at risk (in millions), by species and region

Region	Cattle	Pigs	Goats	Sheep	Buffalo	Total
East Asia and the Pacific	63.2	190.9	79.9	108.1	0.24	442.4
South Asia	61.6	1.8	72.5	18.7	0.33	154.8
Western and Central Europe	22.2	60.9	7.5	42.2	<0.1	132.8
North Africa and the Middle East	15.8	0.2	13.4	65.2	<0.1	94.6
Eastern Europe and Central Asia	26.6	12.0	8.9	40.4	<0.1	87.8
Sub-Saharan Africa	30.5	5.3	22.4	14.5	0	72.8
Latin America and the Caribbean	21.9	8.0	5.7	8.1	0	43.7
North America	23.0	15.2	0.45	0.29	0	39.0
Australia and Oceania	3.1	0.61	0.47	22.7	0	26.9
World total	**268.1**	**294.9**	**211.2**	**320.1**	**0.58**	**1,094.9**

populations[1,23]. We note that several ungulate species could probably benefit from improved epizootic surveillance, given range overlap with anthrax and limited coverage by protected areas, which are a foundation of anthrax surveillance and control for most wildlife (Table 3)[24]. Saiga antelope (*Saiga tatarica*) in particular have a significant overlap with anthrax outside protected parts of their range, and the recent mass die-off of a third of the entire population of saiga in three weeks highlights the vulnerability of threatened ungulates to sudden, disease-induced population crashes. The anthrax vaccine may be used by conservationists in special cases (for example, with cheetahs and rhinoceros[25]), but the lack of an oral anthrax vaccine makes mass vaccination more impractical for wildlife than for livestock, making surveillance all the more important.

Discussion

Our study has produced a global map of *B. anthracis* suitability as a proxy for anthrax risk, and while this is a major step forward, several important directions remain to make these models actionable for public health practitioners. Although some estimates have been proposed for the annual global burden of anthrax, these estimates range by several orders of magnitude. Most regional assessments, especially in rural Africa, agree that anthrax cases are severely under-reported despite mandatory reporting. Similar studies to ours have used suitability maps to extrapolate global case burden for diseases such as dengue fever or melioidosis (*Burkholderia pseudomallei*)[26,27]; however, this approach seems inadequate for anthrax, given that human incidence is just as strongly determined by anthrax dynamics in wildlife, local agricultural intensity, knowledge about anthrax transmission, access to healthcare and vaccination, and complicating factors such as food insecurity. At national and local levels, One Health approaches to surveillance have had promising results, but a more globally coordinated network among these programmes might help address some of the major data gaps.

Regional-scale modelling will also help advance modelling work that explicitly predicts seasonal dynamics of anthrax risk. Across countries and continents, anthrax dynamics are often seasonal, although this may range from predictable annual outbreaks to sporadic, high-mortality epizootics[12,23,28–31]. The timing and intensity of seasonality are far from consistent across space, even on the same continent[1,5], and the underlying drivers are a complex product of local climate and soil conditions, herbivore community structure and seasonal movement dynamics, and co-morbidity with other pathogens[23,32–34]. Several recently advanced spatiotemporal modelling methods can capture and infer complex seasonal drivers of zoonotic spillover[35,36], but in application to anthrax, these models would be most appropriate at spatial scales where these drivers are consistent across the landscape[37]. Advancing these types of model may help identify spatial patterns of risk that are missing in a static, global map of suitability (including places epizootics may be possible despite a lack of long-term suitability for anthrax establishment), and will also further connect public health work to enzootic versus epizootic dynamics in wildlife. Our work—and future models incorporating more temporally dynamic environmental predictors of anthrax risk—also set a foundation for investigating how climate and land cover change will impact the distribution and burden of anthrax. Published work suggests that anthrax suitability may decrease in parts of Kazakhstan and the southern United States in a changing climate, but other work anticipates warming-driven emergence at higher latitudes[38,39]. Our study includes recent records from the Yamalo-Nenets area of Russia, where outbreaks in reindeer have led to massive economic losses and threaten the livelihood of traditional pastoralists. However, our model made limited predictions of suitability in the sub-Arctic in current

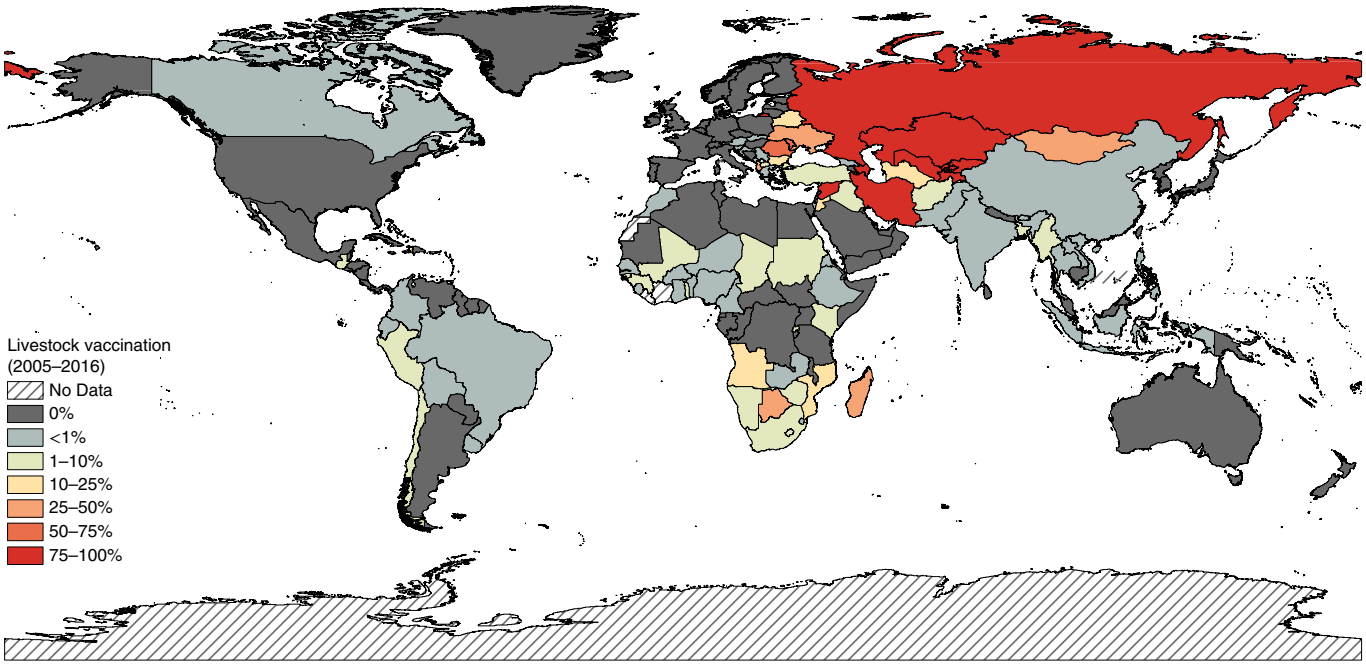

Fig. 3 | Map of average anthrax vaccination rates per country for all livestock species. Average vaccination rates for all livestock (cattle, sheep, goats, buffalo and pigs) reported to the World Animal Health Information System over the interval 2005–2016, as a function of doses administered and reported livestock populations at risk, excluding years with no reported vaccination.

Table 3 | Overlap between selected wildlife species of concern and the global distribution of anthrax, including overlap with the protected areas database

Wildlife species	Geographic overlap	Anthrax-suitable-area overlap with protected areas	IUCN Red List status
Bison (*B. bison*)	32.2%	64.6%	NT
Pronghorn (*A. americana*)	26.6%	3.9%	LC
Roan (*H. equinus*)	23.9%	30.5%	LC
Saiga (*S. tatarica*)	17.5%	2.8%	CE (A2acd)
Moose (*A. alces*)	6.0%	9.9%	LC
Reindeer (*R. tarandus*)	1.6%	14.9%	LC
Yak (*B. mutus*)	0.7%	0%	VU (C10)

IUCN abbreviations: LC, least concern; NT, near threatened; VU, vulnerable; CE, critically endangered; additional information gives reference codes for endangered designation within sections of the IUCN Red List.

climates. Even though anthrax cases are regularly reported throughout Sweden, northern Russia and other cold, high-latitude countries, high-latitude outbreaks are proportionally under-represented in our database (and are often poorly documented). Persistence at higher latitudes may also be better predicted by a slightly different set of climatic constraints on persistence. A recently published model trained on high-latitude cases in the Northern Hemisphere seems to underpredict known areas of endemism in warmer climates, possibly supporting this explanation[39]. Feedback between local modelling efforts and updated global consensus mapping will improve our overall understanding of what drives different anthrax dynamics, and the likely impact of climate change.

Finally, we observe increasing interest, by microbiologists and ecologists alike, in the closely related 'anthrax-like' *Bacillus cereus* biovar. *anthracis* (*Bcbva*). Whereas *B. cereus* is a typically non-pathogenic soil bacterium, the pathogenic *Bcbva* carries variants of the pXO1 and pXO2 plasmids that allow capsule production, which are both required for full virulence in *B. anthracis*. A recent study in Taï National Park in Cote D'Ivôire showed that *Bcbva* accounted for 40% of wildlife mortality in a 26-year survey, and could potentially drive the local extinction of chimpanzees in the Taï Forest within the next century[40]. The geographic distribution of *Bcbva* is still unknown, and it is plausible that different climatic and environmental factors determine the spatial patterns of its transmission; however, improved diagnostics will be necessary to differentiate the role of the two pathogens in anthrax infections beyond Taï National Park. Mapping *Bcbva* across West Africa may be an important next step for measuring the threat of anthrax and anthrax-like disease to wildlife conservation (and, potentially, to human health in the future).

Methods

Occurrence and pseudoabsence data. We assembled a global occurrence database for *B. anthracis* out of a combination of outbreak data collected in the field by the authors or their extended team of collaborators, national passive surveillance and reporting infrastructures, online records from ProMed Mail, and georeferenced records or digitized maps from peer-reviewed publications documenting anthrax outbreaks. Our final database of 5,018 unique records spanning 70 countries and more than a century (1914–2018) thinned to 2,310 distinct localities after removing uncertain sightings and thinning to a single point per unique 10 arcmin (~20 km at the Equator) cell, to correct for sampling bias[41]. For background environmental data, a total dataset of 10,000 pseudoabsences were randomly generated from countries where anthrax occurrence records were collected, an upper sample commonly used for similar disease distribution mapping studies[42]. Of these 10,000, an equal 1:1 sample was randomly selected to match the presence points in submodels, as is recommended for BRT models[43].

Environmental predictors. Global layers of environmental predictors were selected on the basis of successful variables used in previously published anthrax distribution modelling studies at regional scales[13–15], as well as from other distribution modelling studies on soil-borne pathogens[27]. Climate data were taken from version 1.4 of the WorldClim dataset, which includes 19 bioclimatic variables characterizing average and seasonal trends in temperature and precipitation[44].

In addition to climate data, we included layers describing elevation, soil and two vegetation indices. Elevational data were taken from the Global Multi-resolution Terrain Elevation Data (GMTED2010) dataset provided by the US Geological Service. Soil layers were taken from the Global Soil Information Facilities SoilGrids database at 250 m resolution; four layers were included: soil pH, and the predicted soil content of sand, humult and calcic vertisols at a depth of 0–5 cm[45]. The mean and amplitude of the normalized difference vegetation index were taken from the Trypanosomiasis and Land Use in Africa (TALA) dataset[46]. To prevent overfitting and reduce correlation among predictor variables, the variable set was reduced down using an automated procedure within the BRT implementation.

Distribution modelling. BRTs are currently considered a best practices method for modelling the global distribution of infectious diseases[26,47], including other soil-transmitted pathogens such as *B. pseudomallei*[27]. In our study, BRTs were implemented using the 'gbm' package in R to develop a global species distribution model for *B. anthracis*. Automated variable set reduction procedures selected a total of 17 predictor layers: 10 bioclimatic variables, 2 vegetation indices, elevation and 4 soil variables. Presence, absence and environmental data were run through the 'gbm.step' procedure on default settings (tree complexity = 4, learning rate = 0.005), following the established template of other studies. A total of 500 submodels were run; for each, presence points were bootstrapped, and pseudoabsences were randomly selected from the total 10,000 to achieve a 1:1 ratio[43]. Separate from the internal cross-validation (75%–25% split) of the BRT procedure, both presence and pseudoabsence points were split into an 80% training and 20% test dataset in each submodel, and model AUC was evaluated on the basis of the independent test dataset. A final average model was calculated across the 500 submodels, and the 5th and 95th percentiles were retained for use in the population at risk analyses. Models performed very well on the withheld test data (mean submodel AUC = 0.9244).

Estimation of human and livestock populations at risk. We estimated the vulnerability of human and livestock populations by overlaying population datasets with maps of anthrax-suitable areas[28]. We mapped global anthrax suitability by dichotomizing model predictions with a threshold of 0.565 for suitable versus unsuitable predictions, with the threshold selected to maximize the true skill statistic (which weights sensitivity and specificity equally) of mean predictions across the entire dataset of all sightings and pseudoabsences. We estimated global population at risk using human population counts for 2015 from the Gridded Population of the World dataset, version 4.0. We dichotomized 'urban' and 'rural' areas using the Global Human Built-up and Settlement Extent dataset, version 1.0. We further split 'urban' areas into urban and peri-urban on the basis of the Gridded Population of the World dataset, where we used a density under 1,000 people per square kilometre as the threshold for classification as peri-urban. To measure possible occupational exposure, we used a global dataset of rural poor livestock keeper density[48]. Finally, we estimated the number of livestock (cattle, sheep, goats and swine) using a database of global livestock density at a spatial resolution of ~1 km × 1 km (https://livestock.geo-wiki.org/home-2/)[49]. Those livestock populations at risk were further stratified by each of the livestock production zones using the livestock production systems data version 5 (https://livestock.geo-wiki.org/home-2/)[48–50]. For all human and livestock analyses, we obtained vulnerability estimates by overlaying population counts with dichotomized anthrax-suitable areas from the BRT models; 95% credibility intervals were calculated by using the 5% (lower) and 95% (upper) bounds of the averaged BRT model prediction, in place of the mean prediction[28].

Delineating wildlife at risk. We evaluated overlap between range maps of every extant ungulate with International Union for Conservation of Nature (IUCN) conservation status (Artiodactyla and Perissodactyla; after reducing from all mammals in IUCN—see Supplementary Information). We identified ungulate species of interest on the basis of species of conservation concern with known range overlap with anthrax, and measured the degree of range overlap with our global *B. anthracis* model, as a proxy for anthrax exposure. We selected seven candidate species of interest for the main analysis: pronghorn (*Antilocapra americana*), roan (*Hippotragus equinus*), saiga (*S. tatarica*), moose (*Alces alces*), reindeer (*Rangifer tarandus*), wild yak (*Bos mutus*) and bison (*Bison bison*). Of the seven, saiga are most threatened, and are listed on the IUCN Red List as critically endangered. Yak are listed as vulnerable; bison are listed as near threatened; and pronghorn, roan and moose are listed as least concern. We use the World Database on Protected Areas and official IUCN range maps, although we note that these range maps tend to overestimate ranges and can be misleading for conservation work[51]. (At least for saiga, we note that telemetry studies are currently underway to reassess the boundaries of the species' range.)

Reporting Summary. Further information on research design is available in the Nature Research Reporting Summary linked to this article.

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request and approval from appropriate partner country ministries of health or agriculture.

Received: 7 September 2018; Accepted: 22 March 2019;
Published online: 13 May 2019

References

1. Carlson, C. J. et al. Spores and soil from six sides: interdisciplinarity and the environmental biology of anthrax (*Bacillus anthracis*). *Biol. Rev.* **93**, 1813–1831 (2018).
2. Swartz, M. N. Recognition and management of anthrax—an update. *N. Engl. J. Med.* **345**, 1621–1626 (2001).
3. *Anthrax in Humans and Animals* (World Health Organization and International Office of Epizootics, 2008).
4. Alexander, K. A., Lewis, B. L., Marathe, M., Eubank, S. & Blackburn, J. K. Modeling of wildlife-associated zoonoses: applications and caveats. *Vector-Borne Zoonotic Dis.* **12**, 1005–1018 (2012).
5. Hugh-Jones, M. & Blackburn, J. The ecology of *Bacillus anthracis*. *Mol. Aspects Med.* **30**, 356–367 (2009).
6. Hugh-Jones, M. & De Vos, V. Anthrax and wildlife. *Sci. Tech. Rev. Off. Int. Epizoot.* **21**, 359–384 (2002).
7. Turner, W. C. et al. Fatal attraction: vegetation responses to nutrient inputs attract herbivores to infectious anthrax carcass sites. *Proc. R. Soc. Lond. B* **281**, 20141785 (2014).
8. Coleman, M. E., Thran, B., Morse, S. S., Hugh-Jones, M. & Massulik, S. Inhalation anthrax: dose response and risk analysis. *Biosecurity Bioterrorism* **6**, 147–160 (2008).
9. Shadomy, S. et al. *Anthrax Outbreaks: A Warning for Improved Prevention, Control and Heightened Awareness* (EMPRES Watch Vol. 37, FAO, 2016).
10. Blackburn, J. K., Kracalik, I. T. & Fair, J. M. Applying science: opportunities to inform disease management policy with cooperative research within a one health framework. *Front. Public Health* **3**, 276 (2016).
11. Mullins, J. C. et al. Ecological niche modeling of Bacillus anthracis on three continents: evidence for genetic–ecological divergence? *PloS ONE* **8**, e72451 (2013).
12. Chen, W.-J. et al. Mapping the distribution of anthrax in mainland China, 2005–2013. *PLoS Negl. Trop. Dis.* **10**, e0004637 (2016).
13. Mullins, J. et al. Ecological niche modelling of the *Bacillus anthracis* A1. A sub-lineage in Kazakhstan. *BMC Ecol.* **11**, 32 (2011).
14. Blackburn, J. K., McNyset, K. M., Curtis, A. & Hugh-Jones, M. E. Modeling the geographic distribution of *Bacillus anthracis*, the causative agent of anthrax disease, for the contiguous United States using predictive ecologic niche modeling. *Am. J. Trop. Med. Hyg.* **77**, 1103–1110 (2007).
15. Barro, A. S. et al. Redefining the Australian anthrax belt: modeling the ecological niche and predicting the geographic distribution of *Bacillus anthracis*. *PLoS Negl. Trop. Dis.* **10**, e0004689 (2016).
16. Seboxa, T. & Goldhagen, J. Anthrax in Ethiopia. *Trop. Geogr. Med.* **41**, 108–112 (1989).
17. Deribe, K. et al. The burden of neglected tropical diseases in Ethiopia, and opportunities for integrated control and elimination. *Parasites Vectors* **5**, 240 (2012).
18. Pieracci, E. G. et al. Prioritizing zoonotic diseases in Ethiopia using a one health approach. *One Health* **2**, 131–135 (2016).
19. Griffith, J. et al. Investigation of inhalation anthrax case, United States. *Emerg. Infect. Dis.* **20**, 280 (2014).
20. Kracalik, I. et al. Changing patterns of human anthrax in Azerbaijan during the post-Soviet and preemptive livestock vaccination eras. *PLoS Negl. Trop. Dis.* **8**, e2985 (2014).
21. Blackburn, J. K. et al. *Bacillus anthracis* diversity and geographic potential across Nigeria, Cameroon and Chad: further support of a novel West African lineage. *PLoS Negl. Trop. Dis.* **9**, e0003931 (2015).
22. Kracalik, I., Malania, L., Imnadze, P. & Blackburn, J. K. Human anthrax transmission at the urban–rural interface, Georgia. *Am. J. Trop. Med. Hyg.* **93**, 1156–1159 (2015).
23. Hampson, K. et al. Predictability of anthrax infection in the Serengeti, Tanzania. *J. Appl. Ecol.* **48**, 1333–1344 (2011).
24. Clegg, S. Preparedness for anthrax epizootics in wildlife areas. *Emerg. Infect. Dis.* https://doi.org/10.3201/eid1207.060458 (2006).
25. Turnbull, P. et al. Vaccine-induced protection against anthrax in cheetah (*Acinonyx jubatus*) and black rhinoceros (*Diceros bicornis*). *Vaccine* **22**, 3340–3347 (2004).
26. Bhatt, S. et al. The global distribution and burden of dengue. *Nature* **496**, 504–507 (2013).
27. Limmathurotsakul, D. et al. Predicted global distribution of *Burkholderia pseudomallei* and burden of melioidosis. *Nat. Microbiol.* **1**, 15008 (2016).
28. Kracalik, I. T. et al. Modeling the environmental suitability of anthrax in Ghana and estimating populations at risk: implications for vaccination and control. *PLoS Negl. Trop. Dis.* **11**, e0005885 (2017).
29. Munang'andu, H. M. et al. The effect of seasonal variation on anthrax epidemiology in the upper Zambezi floodplain of western Zambia. *J. Vet. Sci.* **13**, 293–298 (2012).

30. Lepheana, R. J., Oguttu, J. W. & Qekwana, D. N. Temporal patterns of anthrax outbreaks among livestock in Lesotho, 2005–2016. *PloS One* **13**, e0204758 (2018).
31. Blackburn, J. K. et al. Modeling the ecological niche of *Bacillus anthracis* to map anthrax risk in Kyrgyzstan. *Am. J. Trop. Med. Hyg.* **96**, 550–556 (2017).
32. Cizauskas, C. A. et al. Gastrointestinal helminths may affect host susceptibility to anthrax through seasonal immune trade-offs. *BMC Ecol.* **14**, 27 (2014).
33. Havarua, Z., Turner, W. C. & Mfune, J. K. Seasonal variation in foraging behaviour of plains zebra (*Equus quagga*) may alter contact with the anthrax bacterium (*Bacillus anthracis*). *Can. J. Zool.* **92**, 331–337 (2014).
34. Zidon, R., Garti, S., Getz, W. M. & Saltz, D. Zebra migration strategies and anthrax in Etosha National Park, Namibia. *Ecosphere* **8**, e01925 (2017).
35. Schmidt, J. P. et al. Spatiotemporal fluctuations and triggers of ebola virus spillover. *Emerg. Infect. Dis.* **23**, 415–422 (2017).
36. Kaul, R. B., Evans, M. V., Murdock, C. C. & Drake, J. M. Spatio-temporal spillover risk of yellow fever in Brazil. *Parasites Vectors* **11**, 488 (2018).
37. Getz, W. M. et al. Making ecological models adequate. *Ecol. Lett.* **21**, 153–166 (2018).
38. Blackburn, J. K. in *Emerging and Endemic Pathogens* (eds O'Connell, K., Skowronski, E., Sulakvelidze A. & Bakanidze, L.) 59–88 (Springer, 2010).
39. Walsh, M. G., de Smalen, A. W. & Mor, S. Climatic influence on the anthrax niche in warming northern latitudes. *Sci. Rep.* **8**, 9269 (2018).
40. Hoffmann, C. et al. Persistent anthrax as a major driver of wildlife mortality in a tropical rainforest. *Nature* **548**, 82–86 (2017).
41. Boria, R. A., Olson, L. E., Goodman, S. M. & Anderson, R. P. Spatial filtering to reduce sampling bias can improve the performance of ecological niche models. *Ecol. Model.* **275**, 73–77 (2014).
42. Nsoesie, E. O. et al. Global distribution and environmental suitability for chikungunya virus, 1952 to 2015. *Euro Surveill.* **21**, 30234 (2016).
43. Barbet-Massin, M., Jiguet, F., Albert, C. H. & Thuiller, W. Selecting pseudo-absences for species distribution models: how, where and how many? *Methods Ecol. Evol.* **3**, 327–338 (2012).
44. Hijmans, R. J., Cameron, S. E., Parra, J. L., Jones, P. G. & Jarvis, A. Very high resolution interpolated climate surfaces for global land areas. *Int. J. Climatol.* **25**, 1965–1978 (2005).
45. Hengl, T. et al. SoilGrids250m: global gridded soil information based on machine learning. *PloS ONE* **12**, e0169748 (2017).
46. Hay, S., Tatem, A., Graham, A., Goetz, S. & Rogers, D. Global environmental data for mapping infectious disease distribution. *Adv. Parasitol.* **62**, 37–77 (2006).
47. Messina, J. P. et al. The global distribution of Crimean-Congo hemorrhagic fever. *Trans. R. Soc. Trop. Med. Hyg.* **109**, trv050 (2015).
48. *Global Livestock Production Systems* (Food and Agriculture Organization of the United Nations, 2011).
49. Robinson, T. P. et al. Mapping the global distribution of livestock. *PLoS ONE* **9**, e96084 (2014).
50. Thornton, P. *Mapping Poverty and Livestock in the Developing World* (ILRI, 2002).
51. Ramesh, V., Gopalakrishna, T., Barve, S. & Melnick, D. J. IUCN greatly underestimates threat levels of endemic birds in the Western Ghats. *Biol. Conserv.* **210**, 205–221 (2017).

Acknowledgements

The authors thank D. Pigott for helpful tips on BRT modelling; A. Barner for help obtaining World Animal Health Information System vaccination data; S. J. Ryan for general feedback and technical support; G. Simpson for visualization advice; P. Thornton for access to the global dataset of rural poor livestock keepers; T. A. Joyner for data support; and countless livestock and wildlife managers, clinicians and field technicians for contributing data points. Partial funding for this study was provided by NIH 1R01GM117617-01 to J.K.B. and W.M.G. C.J.C. was supported by the National Socio-Environmental Synthesis Center (SESYNC) under funding received from the National Science Foundation DBI-1639145. K.A. was supported in part under the National Science Foundation (NSF EEID grant 1518663). We also thank the Botswana Government Department of Wildlife and National Parks for their assistance and active collaboration on research directed at understanding Botswana anthrax dynamics.

Author contributions

C.J.C., I.T.K. and J.K.B. conceived of the study. J.K.B., M.E.H.-J., I.T.K. and C.J.C. collected and georeferenced data. C.J.C., I.T.K. and J.K.B. designed the models, and C.J.C. ran models and analyses. N.R. contributed R code. All authors contributed to the writing and editing of the draft and approved the study before submission.

Competing interests

The authors declare no competing interests.

Additional information

Supplementary information is available for this paper at https://doi.org/10.1038/s41564-019-0435-4.

Reprints and permissions information is available at www.nature.com/reprints.

Correspondence and requests for materials should be addressed to J.K.B.

Publisher's note: Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

nature research

Corresponding author(s): Blackburn, Jason K.

Reporting Summary

Nature Research wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Research policies, see Authors & Referees and the Editorial Policy Checklist.

Statistical parameters

When statistical analyses are reported, confirm that the following items are present in the relevant location (e.g. figure legend, table legend, main text, or Methods section).

n/a	Confirmed	
☐	☒	The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒	An indication of whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒	The statistical test(s) used AND whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☐	☒	A description of all covariates tested
☐	☒	A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒	A full description of the statistics including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☒	☐	For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☒	☐	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☐	☒	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☒	☐	Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated
☒	☐	Clearly defined error bars *State explicitly what error bars represent (e.g. SD, SE, CI)*

Our web collection on statistics for biologists may be useful.

Software and code

Policy information about availability of computer code

Data collection	All collation was performed in either ArcGIS version 10 or in R using publicly available packages. All packages are defined in the narrative and supplement in detail.
Data analysis	All analyses were performed in R or ArcGIS and versions and packages are clearly presented in each the text and a very detailed supplementary document. All Code in R can be made available.

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors/reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A list of figures that have associated raw data
- A description of any restrictions on data availability

The data in the study were compiled from several sources and are compiled in the supplemental information and Figure 1 and supplementary figures of data points.

Some data in the US were provided under specific data sharing agreements that require permission from the land owner to share. Requests for data can be made to the corresponding author.

Field-specific reporting

Please select the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☐ Life sciences ☐ Behavioural & social sciences ☒ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/authors/policies/ReportingSummary-flat.pdf

Ecological, evolutionary & environmental sciences study design

All studies must disclose on these points even when the disclosure is negative.

Study description	Briefly, we developed a state-of-the-art species distribution model of Bacillus anthracis, the causative agent of anthrax. We used a boosted regression tree modeling framework and outbreak data from the open literature, our own historical work, and data shared by colleagues of the senior author. We modeled the potential geographic distribution of the pathogen and overlaid the populations of humans and livestock at risk to determine the public health demand. We also overlaid risk areas with distributions of rare wildlife to determine where surveillance should be prioritized.
Research sample	Our outbreak data were compiled from open literature, historical records compiled by the authors, a long history of outbreak mapping by Hugh-Jones, Blackburn, and other co-authors, and online reports from reporting systems like ProMedMail. Our data were idiosyncratic in collection, a common situation for species distribution modeling. We used averaged climate variables to address the time span of outbreak data, a common solution for such modeling efforts.
Sampling strategy	We have assembled the largest known database of anthrax outbreak locations for this study. Our goal was reach as close to global coverage as possible. We identify limitations of this sampling within the study in the narrative and supplement and provide details on the collection of data from each location.
Data collection	The data collection was a joint effort of the author team, lead by the senior author. We had a historical database of outbreaks from various studies and historical anthrax outbreak reports. In this study, we compiled these into a single GIS database for modeling within a BRT framework. Environmental data were publicly available and the sources are provided to the readers in detail.
Timing and spatial scale	The outbreaks span several decades with the majority of data from the early 2000s to present. This is an idiosyncratic database, typical of species distribution modeling studies. The modeling approach results in presence/absence predictions at the spatial scale of the environmental variables (10 arcmin). We disaggregated these models to 2.5 arcminute to match resolution of human population data to determine populations at risk in the modeled anthrax zone. Climate data from Worldclim are averaged over a 50 year period (based on ecological niche theory that the niche is adapted to the mean phenotype of a population). Other environmental data were derived from satellite data (e.g. NDVI over a multi-year period of ~5 years).
Data exclusions	For this study, outbreak data were filtered to a single event per spatial unit at the scale of 10 arcminute to avoid over sampling in the random draws of point for training/testing. This filtering process is described in detail.
Reproducibility	We reran all models repeatedly and compare results. Results were stable overall. We also performed a model averaging approach so we could share our estimate of error in the supplement.
Randomization	Our modeling approach involved iterative sampling of outbreak and pseudo-absence points (methodology for defining these is provided) to run multiple models before arriving at the final models presented in the paper.
Blinding	This study relied on outbreak data to model the overall global geographic distribution of a pathogen. There was not application of sample blinding required.

Did the study involve field work? ☐ Yes ☒ No

Reporting for specific materials, systems and methods

Materials & experimental systems

n/a	Involved in the study
☒	☐ Unique biological materials
☒	☐ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology
☒	☐ Animals and other organisms
☒	☐ Human research participants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging